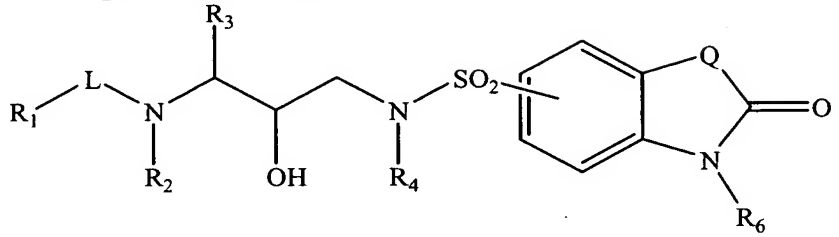
CLAIMS

1. A compound having the formula

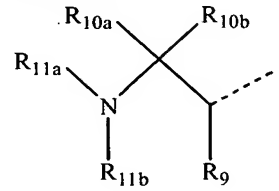


(I)

an *N*-oxide, salt, stereoisomeric form, racemic mixture, prodrug, ester or metabolite thereof, wherein

R_1 and R_8 are, each independently, hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, arylC_{1-6}alkyl, C_{3-7}cycloalkyl, C_{3-7}cycloalkylC_{1-6}alkyl, aryl, Het^1, Het^1C_{1-6}alkyl, Het^2, Het^2C_{1-6}alkyl;

R_1 may also be a radical of formula



(II)

wherein

R_9, R_{10a} and R_{10b} are, each independently, hydrogen, C_{1-4}alkyloxycarbonyl, carboxyl, aminocarbonyl, mono- or di(C_{1-4}alkyl)aminocarbonyl, C_{3-7}cycloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl or C_{1-6}alkyl optionally substituted with aryl, Het^1, Het^2, C_{3-7}cycloalkyl, C_{1-4}alkyloxycarbonyl, carboxyl, aminocarbonyl, mono- or di(C_{1-4}alkyl)aminocarbonyl, aminosulfonyl, C_{1-4}alkyl$S(O)_t$, hydroxy, cyano, halogen or amino optionally mono- or disubstituted where the substituents are each independently selected from C_{1-6}alkyl, aryl, arylC_{1-4}alkyl, C_{3-7}cycloalkyl, C_{3-7}cycloalkylC_{1-4}alkyl, Het^1, Het^2, Het^1C_{1-4}alkyl and Het^2C_{1-4}alkyl; wherein R_9, R_{10a} and the carbon atoms to which they are attached may also form a C_{3-7}cycloalkyl radical; when L is -O–C_{1-6}alkanediyl-C(=O)- or -NR_8-C_{1-6}alkanediyl-C(=O)-, then R_9 may also be oxo;

R_{11a} is hydrogen, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-7}cycloalkyl, aryl, aminocarbonyl optionally mono- or disubstituted, aminoC_{1-4}alkylcarbonyloxy optionally mono- or disubstituted, C_{1-4}alkyloxycarbonyl, aryloxycarbonyl, Het^1oxycarbonyl, Het^2oxycarbonyl, aryloxycarbonylC_{1-4}alkyl, arylC_{1-4}alkyloxycarbonyl, C_{1-4}alkylcarbonyl, C_{3-7}cycloalkylcarbonyl, C_{3-7}cycloalkylC_{1-4}alkyloxycarbonyl, C_{3-7}cycloalkylcarbonyloxy,

carboxylC_{1-4}alkylcarbonyloxy, C_{1-4}alkylcarbonyloxy, arylC_{1-4}alkyl-carbonyloxy, arylcarbonyloxy, aryloxycarbonyloxy, Het^{1}carbonyl, Het^{1}carbonyloxy, Het$^1C_{1-4}$alkyloxycarbonyl, Het^{2}carbonyloxy, Het$^2C_{1-4}$alkylcarbonyloxy, Het$^2C_{1-4}$alkyloxycarbonyloxy or C_{1-6}alkyl optionally substituted with aryl, aryloxy, Het^2 or hydroxy; wherein the substituents on the amino groups are each independently selected from C_{1-6}alkyl, aryl, arylC_{1-4}alkyl, C_{3-7}cycloalkyl, C_{3-7}cycloalkylC_{1-4}alkyl, Het^1, Het^2, Het$^1C_{1-4}$alkyl and Het$^2C_{1-4}$alkyl;

R_{11b} is hydrogen, C_{3-7}cycloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, aryl, Het^1, Het^2 or C_{1-6}alkyl optionally substituted with halogen, hydroxy, C_{1-4}alkylS(=O)$_t$, aryl, C_{3-7}cycloalkyl, Het^1, Het^2, amino optionally mono- or disubstituted where the substituents are each independently selected from C_{1-4}alkyl, aryl, arylC_{1-4}alkyl, C_{3-7}cycloalkyl, C_{3-7}cycloalkylC_{1-4}alkyl, Het^1, Het^2, Het$^1C_{1-4}$alkyl and Het$^2C_{1-4}$alkyl;

wherein R_{11b} may be linked to the remainder of the molecule via a sulfonyl group;

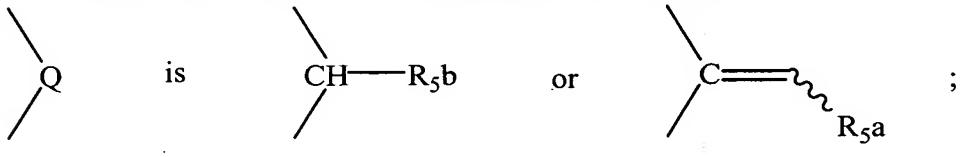
t is, each independently, zero, 1 or 2;

R_2 is hydrogen or C_{1-6}alkyl;

L is -C(=O)-, -O-C(=O)-, -NR$_8$-C(=O)-, -O–C_{1-6}alkanediyl-C(=O)-, -NR$_8$-C_{1-6}alkanediyl-C(=O)-, -S(=O)$_2$-, -O-S(=O)$_2$-, -NR$_8$-S(=O)$_2$, wherein either the C(=O) group or the S(=O)$_2$ group is attached to the NR$_2$ moiety; and wherein each independently the C_{1-6}alkanediyl moiety may be optionally substituted with hydroxy, aryl, Het^1 or Het^2;

R_3 is C_{1-6}alkyl, aryl, C_{3-7}cycloalkyl, C_{3-7}cycloalkylC_{1-4}alkyl, or arylC_{1-4}alkyl;

R_4 is hydrogen, C_{1-4}alkyloxycarbonyl, carboxyl, aminocarbonyl, mono- or di(C_{1-4}alkyl)aminocarbonyl, C_{3-7}cycloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl or C_{1-6}alkyl optionally substituted with one or more substituents each independently selected from aryl, Het^1, Het^2, C_{3-7}cycloalkyl, C_{1-4}alkyloxycarbonyl, carboxyl, aminocarbonyl, mono- or di(C_{1-4}alkyl)aminocarbonyl, aminosulfonyl, mono- or di(C_{1-4}alkyl)aminosulfonyl, C_{1-4}alkylS(=O)$_t$, hydroxy, cyano, halogen or amino optionally mono- or disubstituted where the substituents are each independently selected from C_{1-4}alkyl, aryl, arylC_{1-4}alkyl, C_{3-7}cycloalkyl, C_{3-7}cycloalkylC_{1-4}alkyl, Het^1, Het^2, Het$^1C_{1-4}$alkyl and Het$^2C_{1-4}$alkyl;



;

R_{5a} and R_{5b} are, each independently, selected from hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-7}cycloalkyl, aryl, Het^1, Het^2; wherein each of the substituents selected from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl or C_{3-7}cycloalkyl, are optionally substituted on one or more carbon atoms with a substituent independently selected from the group consisting of amino, mono- or di(C_{1-4}alkyl)amino, hydroxy, carboxyl, oxo, mercapto, halogen, cyanogen, nitro, C_{1-4}alkyloxy, C_{1-4}alkylcarbonyl, C_{1-4}alkylcarbonyloxy, C_{1-4}alkyloxycarbonyl, aryl, C_{3-7}cycloalkyl, Het^1, Het^2, C_{1-4}alkylcarbonyloxy, C_{1-4}alkyloxycarbonyl;

R_6 is hydrogen or C_{1-6}alkyl optionally substituted on one ore more carbon atoms with one or more substituents independently selected from the group consisting of amino, mono- or di(C_{1-4}alkyl)amino, hydroxy, mercapto, oxo, cyanogen, nitro, halogen, carboxyl C_{1-4}alkyloxy, C_{1-4}alkylcarbonyl, C_{1-4}alkylcarbonyloxy, C_{1-4}alkyloxycarbonyl, C_{3-7}cycloalkyl, aryl, Het^1, Het^2; wherein each C_{1-4}alkyl may optionally be substituted by amino, mono- or di(C_{1-4}alkyl)amino, hydroxy, mercapto, oxo, cyanogen, nitro, halogen, carboxyl.

2. A compound according to claim 1 wherein R_1 hydrogen, C_{1-6}alkyl, C_{2-6}alkenyl, arylC_{1-6}alkyl, C_{3-7}cycloalkyl, C_{3-7}cycloalkylC_{1-6}alkyl, aryl, Het^1, Het^1C_{1-6}alkyl, Het^2, Het^2C_{1-6}alkyl; wherein Het^1 is a monocyclic or bicyclic heterocycle having 5 to 10 ring members, which contains one or more heteroatom ring members each independently selected from nitrogen, oxygen or sulfur and which is optionally substituted on one or more carbon atoms.

3. A compound according to claim 1 or 2 wherein L is -O–C_{1-6}alkanediyl-C(=O)-.

4. A compound according to any one of claims 1 to 3 wherein

R_{5a} and R_{5b} are each independently selected from the group consisting of aryl, Het^1, Het^2 or C_{1-6}alkyl optionally substituted on one or more atoms with a substituent independently selected from the group consisting of amino, hydroxy, carboxyl, oxo, sulfhydryl, halogen, nitro, cyanogen, C_{1-4}alkyl, aminoC_{1-4}alkyl, hydroxyC_{1-4}alkyl, haloC_{1-4}alkyl, C_{1-4}alkyloxy, C_{1-4}alkylcarbonyl, C_{1-4}alkylcarbonyloxy, C_{1-4}alkyloxycarbonyl, C_{1-4}alkylcarbonyloxyC_{1-4}alkyl, C_{1-4}alkyloxycarbonylC_{1-4}alkyl, aryl, C_{3-7}cycloalkyl, Het^1 and Het^2;

R_6 is hydrogen.

5. A compound according to claim 1 wherein the compound is

(1-Benzyl-2-hydroxy-3-{isobutyl-[2-oxo-3-(1H-pyrrol-2-ylmethylene)-2,3-dihydro-1H-indole-5-sulfonyl]-amino}-propyl)-carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester

(1-Benzyl-2-hydroxy-3-{isobutyl-[3-(5-methyl-furan-2-ylmethylene)-2-oxo-2,3-dihydro-1H-indole-5-sulfonyl]-amino}-propyl)-carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester

(1-Benzyl-2-hydroxy-3-{isobutyl-[3-(5-methyl-thiophen-2-ylmethylene)-2-oxo-2,3-dihydro-1H-indole-5-sulfonyl]-amino}-propyl)-carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester

(1-Benzyl-2-hydroxy-3-{isobutyl-[3-(1-methyl-1H-pyrrol-2-ylmethylene)-2-oxo-2,3-dihydro-1H-indole-5-sulfonyl]-amino}-propyl)-carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester

(1-Benzyl-3-{[3-(2-ethyl-butylidene)-2-oxo-2,3-dihydro-1H-indole-5-sulfonyl]-isobutyl-amino}-2-hydroxy-propyl)-carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester

{1-Benzyl-2-hydroxy-3-[isobutyl-(3-isobutylidene-2-oxo-2,3-dihydro-1H-indole-5-sulfonyl)-amino]-propyl}-carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester

{1-Benzyl-3-[(3-furan-2-ylmethylene-2-oxo-2,3-dihydro-1H-indole-5-sulfonyl)-isobutyl-amino]-2-hydroxy-propyl}-carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester

(1-Benzyl-2-hydroxy-3-{isobutyl-[3-(4-methoxy-benzylidene)-2-oxo-2,3-dihydro-1H-indole-5-sulfonyl]-amino}-propyl)-carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester

(1-Benzyl-2-hydroxy-3-{isobutyl-[2-oxo-3-(4-pyridin-2-yl-benzylidene)-2,3-dihydro-1H-indole-5-sulfonyl]-amino}-propyl)-carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester

(1-Benzyl-2-hydroxy-3-{[3-(4-hydroxy-3,5-dimethyl-benzylidene)-2-oxo-2,3-dihydro-1H-indole-5-sulfonyl]-isobutyl-amino}-propyl)-carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester

(1-Benzyl-3-{[3-(4-dimethylamino-benzylidene)-2-oxo-2,3-dihydro-1H-indole-5-sulfonyl]-isobutyl-amino}-2-hydroxy-propyl)-carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester

(1-Benzyl-2-hydroxy-3-{[3-(1H-indol-2-ylmethylene)-2-oxo-2,3-dihydro-1H-indole-5-sulfonyl]-isobutyl-amino}-propyl)-carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester

Acetic acid 5-(5-{[3-(hexahydro-furo[2,3-b]furan-3-yloxycarbonylamino)-2-hydroxy-4-phenyl-butyl]-isobutyl-sulfamoyl}-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-furan-2-ylmethyl ester

{1-Benzyl-3-[(3-benzylidene-2-oxo-2,3-dihydro-1H-indole-5-sulfonyl)-isobutyl-amino]-2-hydroxy-propyl}-carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester

(1-Benzyl-3-{[3-(4-diethylamino-3-hydroxy-benzylidene)-2-oxo-2,3-dihydro-1H-indole-5-sulfonyl]-isobutyl-amino}-2-hydroxy-propyl)-carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester

(1-Benzyl-2-hydroxy-3-{[3-(2-hydroxy-benzylidene)-2-oxo-2,3-dihydro-1H-indole-5-sulfonyl]-isobutyl-amino}-propyl)-carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester

(1-Benzyl-2-hydroxy-3-{isobutyl-[3-(2-methoxy-benzylidene)-2-oxo-2,3-dihydro-1H-indole-5-sulfonyl]-amino}-propyl)-carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester

(1-Benzyl-3-{isobutyl-[3-(5-methyl-furan-2-ylmethylene)-2-oxo-2,3-dihydro-1H-indole-5-sulfonyl]-amino}-2-phosphonooxy-propyl)-carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester

(1-Benzyl-2-hydroxy-3-{[3-(4-hydroxy-3-methoxy-benzylidene)-2-oxo-2,3-dihydro-1H-indole-5-sulfonyl]-isobutyl-amino}-propyl)-carbamic acid hexahydro-furo[2,3-b]furan-3-yl ester

4-(5-{[3-(Hexahydro-furo[2,3-b]furan-3-yloxycarbonylamino)-2-hydroxy-4-phenyl-butyl]-isobutyl-sulfamoyl}-2-oxo-1,2-dihydro-indol-3-ylidenemethyl)-benzoic acid

a *N*-oxide or a salt thereof, or a stereoisomeric form thereof.

6. A pharmaceutical composition, comprising an effective amount of at least one compound as claimed in any one of claims 1 to 5, and a pharmaceutically tolerable excipient.

7. A method of inhibiting a protease of a multi-drug resistant retrovirus in a mammal infected with said retrovirus, comprising administering a protease inhibiting amount of a compound according to any one of claims 1 to 5 to said mammal in need thereof.

8. A method of treating or combating infection or disease associated with multi-drug resistant retrovirus infection in a mammal, comprising administering an effective amount of at least one compound according to any one of claims 1 to 5 to said mammal.

9. A method of inhibiting multi-drug resistant retroviral replication, comprising contacting a retrovirus with an effective amount of at least one compound according to any one of claims 1 to 5.

10. A compound as claimed in any one of claims 1 to 5 for use as a medicine.

11. The use of a compound as claimed in any one of claims 1 to 5 in the manufacture of a medicament for treating or combating infection or disease associated with multi-drug resistant retrovirus infection in a mammal.